Remarks/Arguments:

Claims 78-91, presented hereby, are pending. Claims 64-77 are canceled, hereby, without prejudice or disclaimer.

Claims 78-91 correspond to claims 64-77, respectively, including amendments to claims 67-69 and 75 (represented in corresponding claims 81-83 and 89, respectively), as explained below.

The objection to claim 75 is resolved, hereby, by deleting "or" from the claim, as represented in present claim 89.

Reconsideration is requested with respect to the rejection of claims 67-69 under 35 USC 112, second paragraph, for allegedly being indefinite.

Claims 67-69 are revised, hereby, as claims 81-83, respectively. Claim 81 is written in Jepson-type language, and the claim includes the active process language "expressing the peptide." Claim 82 uses the active process language "isolating the peptide." Claim 83, also, uses active process language, i.e., "synthesizing the peptide."

In view of the changes made to the rejected claims, as explained above, withdrawal of the rejection of claims 67-69 under 35 USC 112, 2nd paragraph, is in order.

Claims 64-67 were rejected under 35 USC 112, first paragraph, for allegedly lacking enablement. Reconsideration is requested.

According to the statement of rejection, finding lack of enablement focuses on the *use* aspect of the presently claimed invention, specifically, its use as a "medicament." It is alleged that the specification does not (1) enable *how* to use the medicaments (e.g., dosage amount and

frequency/length of administration) and (2) evidence that the medicament would, in fact, be *useful for its intended purpose.*

The statement of rejection is incorrect with respect to *how* to practice the invention. Page 4, first and second paragraphs, of the specification (English language text) describes how unit doses of the medicament are prepared for administration and the dosage amounts to be administered per day.

With respect to usefulness of the invention (medicament) for its intended purpose, it is alleged that the positive test results reported in the instant application do not correlate with *clinical efficacy.* In other words, it is alleged that one of ordinary skill in the art would have considered the presently claimed invention unlikely to be useful for its intended purpose. The statement of rejection is incorrect.

Attention is respectfully directed to the PTO guidelines concerning invention usefulness, which came into effective in July of 1995. These guidelines apply when the rejection concerns the *use* of the invention, regardless of the section of the statute upon which the rejection relies. Whether the rejection is made under § 112, 1st ¶, based on alleged lack of enablement for "using" the invention is of no moment. In fact, this is made clear in the "Guidelines," themselves; MPEP 706.03(a)(1) is entitled:

> Guidelines For Examination of Applications For Compliance With the Utility Requirements of 35 U.S.C. 101 ***and 35 U.S.C. 112***

Keeping the foregoing in mind, specifically, the guidelines state:

> If the applicant has asserted that the claimed invention is useful for any particular purpose (i.e. a "specific utility") and that assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. Credibility is to be assessed from the perspective of one of ordinary skill in the art *in view of any evidence of record (e.g., data, statements, opinions, references, etc.)* that is relevant to the applicant's assertions.

In the present case, the statement of rejection fails to set forth ***"any evidence of record"*** sufficiently credible to support the allegations of failure to enable. Applicant respectfully submits that the rejection has failed to establish a *prima facie* case for lack of enablement for "using" the invention (with respect to the scope of subject matter claimed), since according to the guidelines:

> A *prima facie* showing must contain the following elements: . . .
> ii) *support* for factual findings relied upon in reaching this conclusion ... [emphasis added]

No ***"support,"*** is provided in the outstanding Office Action for the rejection. As required by the guidelines:

> Office personnel must provide documentary evidence (e.g., scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) as the form of *support* used in establishing the factual basis of a *prima facie* showing . . . . [emphasis added].

No evidence is provided in order to support the rejection for lack of enablement.

Nothing by way of scientific reasoning or evidence is provided in the outstanding Office action to rebut the applicant's assertion of usefulness. Lack of enablement is not established by mere allegations of undue breadth; i.e., that claims read on non-disclosed embodiments. *Horton v. Stevens*, 7 USPQ2d 1245 (BPA&I 1988). Again, with reference to the aforesaid PTO guidelines:

> Office personnel are reminded that they must treat as true a statement of fact an applicant in relation to an asserted utility, unless countervailing *evidence* can be provided that shows one or ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement [emphasis added].

Again, no *"evidence"* is provided in the outstanding Office Action to countervail applicant's statement that the claimed invention has usefulness (i.e., utility) in the treatment of tumors, in general.

The presently claimed invention is directed to one specific molecule, i.e., the peptide of SEQ ID NO. 1. This peptide molecule is a fragment of collagen 18. The presently claimed peptide is a naturally occurring peptide that has been isolated from hemofiltrate.

As described in the instant specification (page 4, ¶3), the presently claimed peptide is useful in all therapeutic applications related to uncontrolled vascular growth. This uncontrolled growth of blood vessels is known as *angiogenesis*.

Another fragment of collagen has been isolated (by a third party) and it is the subject of U.S. patent 6,174,861 (O'Reilly), attached hereto (as Appendix 1). O'Reilly (e.g., Abstract) names this fragment "endostatin." The patent teaches that endostatin is useful for treating angiogenesis-dependent diseases such as cancer (O'Reilly, Abstract).

Attached hereto (as Appendix 2) is a two-page document entitled "multiple alignment." The document contains a multi-sequence alignment showing that the presently claimed peptide (hCol-18) and endostatin (HFcol-Pat) are highly homologous - differing only in their C-terminal parts.

Further attached hereto (as Appendix 3) are two printouts from the website of EntreMed Inc. (www.entremed.com). The teachings of these two printouts evidence that endostatin was the subject of clinical trials in which angiogenesis inhibition was shown to have occurred.

As endostatin and the presently claimed peptide have high sequence homology (Appendices 1 and 2, *infra*), and as endostatin inhibits angiogenesis (Appendix 3, *infra*), one skilled in the art would have reasonably expected the presently claimed peptide to function as did endostatin, i.e., as an angiogenesis inhibitor.

From the in vitro experiments reported in the subject application, one skilled in the art would have recognized that the presently claimed peptide inhibits proliferation of endothelial cells, and, so, clearly indicates antiangiogenic properties. Animal tests customarily used for screening should not be discarded in considerations of human utility. *In re Jolles*, 206 USPQ 885 (CPPA 1980). This indication is confirmed by the clinical trials (described above) with the peptide homolog endostatin (Appendix 3, *infra*).

Favorable action is requested.

Respectfully submitted,

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APPENDIX 1